The 35 U.S.C. §112 Rejection

Claims 1, 2, 5-11 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The rejection is respectfully traversed.

Claim 1 has been amended to recite an attenuated bacterial host comprising a recombinant plasmid that carries a fusion protein construct comprising a gene required for surface exposure and a gene encoding a transactivating protein of human immunodeficiency virus type 1. Applicants submit that the characteristics of the claimed bacterial host have been clearly defined. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 5-11 under 35 U.S.C §112, first paragraph, be withdrawn.

Claims 6-10 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The rejection is respectfully traversed.

Claims 6-10 are drawn to a method of initiating immune responses specific for HIV-1 antigens in an animal by the attenuated bacterial host disclosed herein. Applicants submit that the

specification has provided detailed disclosure and sufficient enablement on the induction of both cellular and humoral anti-HIV-1 immune responses by the claimed attenuated bacterial host (Examples 7-9). Accordingly, Applicants respectfully request that the rejection of claims 6-10 under 35 U.S.C. §112, first paragraph, be withdrawn.

The 35 USC §103(a) Rejections

Claims 1, 2, 5 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over **Brey** et al. in view of **Georgiou** et al. and further in view of **Haseltine** et al., **Kang** and **Rodman**. This rejection is respectfully traversed.

Brey et al. disclosed attenuated strain of bacteria that express malarial antigens. **Georgiou** et al. disclosed recombinant DNAs that are suitable for the expression of heterologous antigen on the surface of an enteric microorganism. However, **Georgiou** et al. did not teach or suggest recombinants expressing the HIV-1 *tat* gene.

Haseltine et al. disclosed a HTLV-III/LAC tat_{III} gene that encoded the HTLV-III/LAV associated trans-acting factor (column 3, lines 21-23). HTLV-III/LAV is the human T cell leukemia virus III

(column 1, lines 21-22). Hence, **Haseltine** et al. taught a gene that is different and distinct from the HIV-1 tat gene disclosed herein. **Haseltine** et al. did not teach or suggest HIV-1 tat gene as claimed herein.

Kang disclosed a baculovirus expression system capable of producing foreign gene proteins at high levels. **Kang** taught the rev, vif and pol proteins of HIV-1. **Kang** did not teach or suggest a HIV-1 tat gene.

Rodman disclosed a natural human IgM antibody reactive against the HIV-1 tat protein. Applicants submit that combining **Brey** et al., **Georgiou** et al. and **Rodman** would not lead one of ordinary skill in the art to the claimed methods. The instant invention is drawn to an HIV-1 tat-expressing attenuated bacterial host that can induce both cellular and humoral anti-HIV-1 immune responses. **Brey** et al., **Georgiou** et al. and **Rodman** did not teach or suggest an HIV-1 tat-expressing bacteria can be used to induce anti-HIV-1 immune responses. Neither did **Brey** et al., **Georgiou** et al. and **Rodman** teach or suggest an HIV-1 tat-expressing attenuated bacterial host can induce both cellular and humoral anti-HIV-1 immune responses as claimed herein. Hence, **Brey** et al., **Georgiou** et al. and **Rodman** do not provide a person having ordinary skill in

this art with the requisite expectation of successfully producing Applicants' claimed invention. The invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 5 and 11 under 35 U.S.C. §103(a) be withdrawn.

Claims 1, 2, 5 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over **Hone** et al. in view of **Georgiou** et al. and further in view of **Haseltine** et al., **Kang** and **Rodman**. This rejection is respectfully traversed.

Hone disclosed an attenuated *Salmonella* vaccine vector containing expression vector encoding HIV-1 gp120 fusion protein. **Georgiou** et al., **Haseltine** et al., **Kang** and **Rodman** have been discussed above. Applicants submit that combining **Hone** et al., **Georgiou** et al. and **Rodman** would not lead one of ordinary skill in the art to the present invention.

The present invention is drawn to an HIV-1 tat-expressing attenuated bacterial host that can induce both cellular and humoral anti-HIV-1 immune responses. **Hone** et al., **Georgiou** et al. and **Rodman** did not teach or suggest tha an HIV-1 tat-

expressing bacteria can be used to induce anti-HIV-1 immune responses. Neither did **Hone** et al., **Georgiou** et al. and **Rodman** teach or suggest an HIV-1 tat-expressing attenuated bacterial host can induce both cellular and humoral anti-HIV-1 immune responses as claimed herein.

Hone et al. only disclosed data on antibody response induced by HIV-1 gp120 fusion protein. **Hone** et al. did not disclose any data on cellular immune response (e.g. T cell response) induced by the HIV-1 gp120 protein. Neither did **Hone** et al. teach or suggest an HIV-1 tat-expressing bacteria can induce both cellular and humoral anti-HIV-1 immune responses as claimed herein. Since induction of cellular and/or humoral immune responses by a putative antigen cannot be predicated and ascertained until actual experiments are carried out in model animals, **Hone** et al., **Georgiou** et al. and **Rodman** do not provide a person having ordinary skill in this art with the requisite expectation of successfully producing Applicants' claimed invention in view of the lack of teaching and suggestion on possible induction of both cellular and humoral immune responses by an HIV-1 tat-expressing bacteria. Thus, the invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly,

Applicants respectfully request that the rejection of claims 1, 2, 5 and 11 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed December 5, 2001. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: June 4, 2002

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